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A STUDY OF ASSOCIATION BETWEEN C-REACTIVE PROTEIN AND FEATURES OF METABOLIC SYNDROME

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ABSTRACT

Objective — To study the clinical profile of patients with metabolic syndrome and find out the association of CRP level with components of the metabolic syndrome.

Research Design And Methods— We conducted a cross-sectional prospective study in 50 cases of metabolic syndrome randomly selected from medical wards of a tertiary care hospital. Total cholesterol (TC), HDL cholesterol, triglycerides, BMI, waist circumference and prevalence of diabetes and hypertension were assessed. To define the metabolic syndrome we used modified ATP III criteria recommended in AHA/NHLBI statement. Complete information for the five variables needed to assess the metabolic syndrome was collected. CRP was measured by latex enhanced immunoturbidimetric assay (high sensitivity CRP assay).

Results— Higher waist circumference cases had higher mean hs-CRP (3.235 Vs 1.950, P <0.0001). Elevated diastolic blood pressure cases had higher mean hs-CRP level (3.264 Vs 2.221, P < 0.05) **Conclusions**—Waist circumference was significantly and independently associated with high hs-CRP levels. The data suggest that hs-CRP value significantly increased with increase in the number of features of metabolic syndrome.

INTRODUCTION

The metabolic syndrome is a constellation of interrelated risk factors of metabolic origin – "metabolic risk factors"- that appear to directly promote the development of atherosclerotic cardiovascular disease.[1] The term metabolic syndrome has been described variously by different groups and various syndromes are also to be found in literature such as syndrome X,[2] deadly quartet, hypertriglycerdemic waist[3] and insulin resistance syndrome. Metabolic syndrome is driving the twin global epidemics of type 2 diabetes and cardiovascular disease. The prevalence of metabolic syndrome is estimated to be around 20-25 per cent of the population globally. People with metabolic syndrome are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome.[4] In addition, almost 200 million people globally have diabetes and 80 percent of these will die from cardiovascular disease,[5] so there is an overwhelming moral, medical and economic imperative to identify these individuals with metabolic syndrome early, so that life style interventions and treatment may prevent the development of diabetes and/or cardiovascular disease.

A number of expert groups have developed clinical criteria for the metabolic syndrome. The most widely accepted of these have

been produced by the WHO, the European group for the study of insulin resistance (EGIR) and NCEP ATP III.[6] All Groups agree on the core components of the metabolic syndrome: obesity, insulin resistance, dyslipidemia and hypertension. However, they apply the criteria differently to identify such a cluster.

Metabolic syndrome and C-reactive protein

People with the metabolic syndrome frequently have a proinflammatory state as shown by elevated cytokines, i.e., TNF and IL-6 and acute phase reactants i.e. CRP, fibrinogen. Estimation of CRP is relatively easy to identify a proinflammatory and inflammatory condition in routine clinical practice. It has been suggested that testing CRP level in blood may be new way to access cardiovascular disease risk, finding of an elevated level support the need for life style changes. Weight reduction may diminish CRP levels and apparently will alleviate the underlying, inflammatory stimulus.

Aims and Objectives

This study was conducted with the following aims and objectives:

1. To study the clinical profile of patients with metabolic syndrome and find out their serum CRP level.
2. To investigate the association of CRP level with components of the metabolic syndrome.

MATERIAL AND METHODS

The present study "A study of association between C-reactive protein and feature of the metabolic syndrome" was conducted at a tertiary care hospital. Permission was taken from the Institutional Ethics Committee. A total of 50 cases of metabolic syndrome were included in the study. Informed consent has been taken in English or local language if applicable. Patients with acute illness were excluded from the study but patients with a history of chronic disease such as ischemic heart disease, malignancy were not excluded. After clinical suspicion, patients underwent detailed interview, clinical examination and investigations. Detailed information was collected about patient's past medical history, dietary habits, life style characteristics, physical activity, tobacco consumption in form of smoking or tobacco chewing and alcohol consumption.

Diagnostic criteria for metabolic syndrome:

Modified ATP III criteria [7, 8] recommended in AHA/ NHLBI statement will be used for diagnosis of metabolic syndrome which is as follows:

Measure (any 3 of 5 constitute diagnosis of metabolic syndrome)	**Categorical cut point**
Elevated waist circumference	>90 cm in male >80 cm in female (for Asian-Indian population)
Elevated triglyceride	> 150 mg/dl or on drug treatment for elevated TG
Reduced HDL cholesterol	< 40 mg/dl in male <50 mg/dl in female or on drug treatment for reduced HDL-C
Elevated BP	>130 mm Hg systolic OR > 85 mm Hg diastolic OR On

	antihypertensive treatment with a history of hypertension
Elevated Fasting glucose	> 100 mg/dl OR On drug treatment for elevated Glucose

To measure waist circumference ,top of right iliac crest was located first and a measuring tape in a horizontal plane was placed around abdomen at iliac crest, tape should not compress the skin and should be parallel to floor. Blood pressure was measured in right upper limb in sitting position noting both systolic and diastolic pressures after a rest of 30 minutes with random zero sphygmomanometer. Patient's height and weight was measured. Body mass index was calculated:

$$\text{BMI } \left(\frac{\text{kg}}{\text{m}^2}\right) = \text{Weight (kg)} \div \text{Height}^2 \text{ (m)}$$

Statistical Analysis

Mean values of CRP was calculated across categorized features of the metabolic syndrome. Spearman's correlation analysis was performed between values for CRP and components of metabolic syndrome. Partial correlation of CRP with categorized features of metabolic syndrome after keeping age and other features constant, analyzed. Cases with different number of features of metabolic syndrome grouped in three groups and difference in mean CRP in these groups was studied.

OBSERVATIONS AND DISCUSSION

We conducted a prospective study in 50 cases of metabolic syndrome randomly selected from medical wards of a tertiary care hospital. To define the metabolic syndrome we used modified ATP III criteria recommended in AHA/NHLBI statement. CRP was measured by latex enhanced immunoturbidimetric assay (high sensitivity CRP assay). Complete information for the five variables needed to assess the metabolic syndrome was collected. Patients with CRP concentration >10 mg/L were not included in our study because such increase may be attributable to condition other than cardiovascular disease.

- Among 50 cases 26 were male and 24 females. All cases were between the ages of 41-70 years. Mean age for males was 56.04 years and for females was 55.54 years.
- Prevalence of tobacco consumption and alcohol consumption was 38% and 22% respectively in our study and 16% cases had both habits.

The utility of hs-CRP in predicting cardiovascular risk has been demonstrated in many studies. In women health study, Ridker et al .found that base line hs-CRP cut point of <1.0 (low risk) ,1.0-3.0 (average risk) and >3 mg/L (high risk) improved predication of relative risk of cardiovascular events (according to the Framingham 10 year risk score) on apparently healthy subjects.

In our study all cases were having $\geq$ 3 features of metabolic syndrome and CRP level $\geq$ 1 mg/L. 31 cases (62%) were at average risk and 19 cases (38%) were at high risk for CVD based on CRP risk criteria.

Among 19 cases with CRP >3 mg/L, 11 were females (58%) and 8 were males (38%). Mean CRP was also higher in

females (3.626) in comparison to males (2.528) with statistically significant difference (P< 0.05).

In our study all the cases with CRP > 3 mg/L had waist circumference above cut off level (≥ 90 in male and ≥ 80 in female) for metabolic syndrome. Mean hs-CRP was also higher in this group than group with less waist circumference with statically significant difference (3.235 Vs 1.950,P<0.0001).

We also found statistically significant difference in mean hs-CRP in the groups based on diastolic blood pressure. Group I with diastolic BP <85 mm Hg had mean hs-CRP 2.221 whereas group II with diastolic BP≥ 85 had mean hs-CRP 3.264 (P<0.05) whereas we didn't find significant difference in mean CRP in groups based on triglyceride level (P=NS), HDL cholesterol level (P=NS), systolic blood pressure (P=NS) and fasting blood sugar (P=NS).

We performed Spearman's correlation analysis between CRP and features of metabolic syndrome. There was a statistically significant unadjusted positive correlation between CRP waist circumference (R= 0.316, P<0.05). Negative correlation was found between CRP and HDL Cholesterol (R= -0.336, P <0.05) and with rest of the features of metabolic syndrome namely TG, SBP , DBP and FBS there was no correlation..

We performed partial correlation of CRP with individual features of metabolic syndrome keeping age and other features constant and found partial correlation of CRP and waist circumference significantly positive (R = 0.422, P< 0.05). There was no correlation of CRP with other features of metabolic syndrome i.e. TG, HDL, SBP, DBP and fasting glucose when adjusted for age and other characters.

In our study all cases were having ≥ 3 features of metabolic syndrome. Therefore, we analyzed CRP values in groups with different number of features. Group I with 3 features, group II with 4 features and group III with 5 features. 46% cases were in group I, 42% were in group II and 12% were in group III. Mean CRP in these three groups respectively 1.813, 3.487, 6.306 was statistically significant (P <0.0001).

CRP varies substantially between people of different ethnic origin and is influenced by their difference in metabolic factors.

Present study was conducted in India and we compared the results with studies conducted in U.K., North America, Europe, China, Japan and South Asians residing in Europe. So, some difference in results can be explained, till more studies are available from our country.

Summary

1. 38% of the cases had hs-CRP level >3 mg/L (High risk for CVD) with female dominance (57.8%).
2. Females had higher mean hs-CRP level in comparison to males (3.626 Vs 2.528 , P <0.05)
3. Higher waist circumference cases had higher mean hs-CRP (3.235 Vs 1.950, P <0.0001). There was significant positive correlation as well as independent partial correlation (P<0.0001) between waist circumference and hs-CRP level.
4. Elevated diastolic blood pressure cases had higher mean hs-CRP level (3.264 Vs 2.221, P < 0.05). There was no crude correlation as well as independent partial correlation between diastolic blood pressure and hs-CRP level.
5. hs-CRP level was not significant affected by systolic blood pressure. There was no crude correlation as well as independent partial correlation between systolic blood pressure and hs-CRP level.
6. hs-CRP level was not significantly affected by high density lipoprotein level. There was negative crude correlation but no independent partial

correlation between high density lipoprotein and hs-CRP.

7. hs-CRP level was not significantly affected by triglyceride level. There was no crude correlation as well as independent partial correlation between triglyceride and hs-CRP level.
8. hs-CRP level was not significantly affected by fasting blood glucose. There was no crude correlation as well as independent partial correlation between fasting blood glucose and hs-CRP level
9. There was statistically highly significant trend (P< 0.001) in hs-CRP level with an increasing number of features of metabolic syndrome.

CONCLUSION

Among the five components (waist circumference, serum triglyceride level, HDL cholesterol, blood pressure and fasting blood glucose) only waist circumference was significantly and independently associated with high hs-CRP levels. Hs-CRP value significantly increased with increase in the number of features of metabolic syndrome.

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